REMARKS/ARGUMENTS

Claims 10 and 11 have been canceled. Claims 1-9 and new Claims 12-16 are active in the case. Reconsideration is respectfully requested.

Applicants' representative wishes to thank Examiners Haghighatian and Kunz for the helpful discussion of October 25, 2004. As a result of the discussion, it is believed that the issues in the case have been clarified and that the prosecution of the application has been materially advanced.

The present invention relates to a polymer for use as an insulating film in the likes of semiconductor devices.

Specification Amendment

The text has been amended at pages 6-7 to correct an obvious omission of a verb from a line of text. Entry of the amendments is respectfully requested.

Claim Amendments

Claims 1-9 have been amended to improve upon the language of the claims. None of the amendments made to the claims introduce new matter into the case.

Basis for new Claims 14 and 15 can be found on page 11 of the specification, while support for Claim 16 can be found on page6 of the text.

Entry of the amendments into the record is respectfully requested.

Claim Rejection, 35 USC 112, second paragraph

The amendments made to Claims 4-6 are believed sufficient to have obviated the issue raised with respect to these claims. Further, Claim 10 has been canceled. Withdrawal of the rejection is respectfully requested.

Invention

The present invention is directed to a stable pharmaceutical formulation for inhalation through nebulisation that consists of a solution of a steroid in which a) the steroid concentration ranges from 0.01 % to 0.1 %, b) the liquid component of the solution is a mixture of water and propylene glycol in a ratio ranging from 60:40 to 30:70 v/v; and c) the pH ranges from 3.5 to 5.0, the pH of the formulation having been adjusted by the addition of a concentrated strong acid to the solution; wherein the percentage of nebulised active ingredient particles with MAD below 6 μm is higher than 70 % and the nebulisation efficiency is higher than 20 %.

Prior Art Rejection

Claims 1-11 stand rejected based on 35 USC 103(a) as obvious over Saidi et al, U. S. Patent 6,241,969 in view of Davis. This ground of rejection is respectfully traversed.

The Davis reference is relevant to the present invention insofar as it discloses the preparation of aqueous solutions of flunisolide in an appropriate solvent which is propylene glycol in order to provide a formulation of the drug that is suitable for administration by nebulization. (A discussion of the reference is found on page 10 of the specification.). On the other hand, there is no teaching or suggestion of an aqueous solution of a steroid in which the constituents of the formulation are a liquid carrier medium of water/propylene glycol and a steroid, where the pH of the solution is adjusted by a strong acid to within the specific range of 3.5 to 5.0. Moreover, not only does the formulation of the present invention provide a nebulizable solution that is stable without the need for stabilizing agents and antioxidants such as metal chelating agents, but adjustment in the pH of the present formulation does not occur as is conventionally done by the addition of saline buffer salts to a pharmacological solution, but rather by the addition of a strong acid such as HCl. In fact, whereas when saline

buffer salts are added to pharmaceutical formulations, assay results for active ingredient(s) usually indicate that within three months there are usually losses of active ingredients of 10 % or higher. On the other hand, by adjustment of pH in the present formulation by a strong acid, surprisingly, assay results remain substantially unchanged in active ingredient levels after 18 months of storage (25°C, 60 % R.H.). Clearly, there is no suggestion whatever of the specific formulation that is claimed in the present invention.

The deficiencies of Davis are neither overcome nor improved upon by Saidi et al. Although the patent discloses a corticosteroid composition intended for administration to the respiratory tract, the formulation disclosed therein is entirely unlike or dissimilar to the composition of the present invention. In Saidi et al, a corticosteroid is formulated with a surfactant having an HLB of a certain level in an aqueous medium that also may contain one or more of buffering agents, tonicity, taste-masking and preservation additives. The Examiner notes that the patent discloses a pH adjustment of the composition to within the range of about 4 to about 8. However, if pH adjustment is accomplished in the composition of the patent, it is done so by the addition of *buffers* such as the usual pharmacological buffering salts to the composition, and ***not*** a strong acid such as HCl. Moreover, the present invention positively excludes the surfactant ingredient of the reference from the present formulation as is clear from the language of the present claims. Clearly, the present composition as claimed is not suggested by the cited combination of references and withdrawal of the rejection is respectfully requested.

Claims 1-11 stand rejected based on 35 USC 103(a) as obvious over Davis in view of Blondino et al, U. S. Patent 6,004,537 in view of Davis. This ground of rejection is respectfully traversed.

As noted in the discussion above, Davis simply describes a nebulizable aqueous solution of flunisolide in an appropriate solvent which is propylene glycol. Nothing, however,

is disclosed of a stable aqueous/propylene glycol, steroid containing solution that is stable over long periods of time without having to add buffering salts and stabilizing and preservative agents to the formulation. Moreover, as noted, the reference mentions nothing of the need to adjust the pH of the formulation that is prepared. There is certainly no suggestion of adding a strong acid such as HCl to the aqueous solution that is described.

The disclosure of Blondino et al describes aerosol formulations of Budesonide/Formoterol in a cosolvent for the active ingredients with at least one fluoroalkane propellant. Such a formulation has nothing to do with the present invention, nor the composition of the Davis reference. In fact, Blondino et al describes the dissolution of the steroid combination in a solvent of a type as described in column 2, lines 52-65, of which a preferred solvent is an aliphatic alcohol, particularly ethanol. (Propylene glycol is not shown or suggested by the patent.) The solution is enclosed in a container which contains the fluorocarbon propellant under pressure. Clearly, one of skill in the art can nor arrive at the present invention as claimed upon consideration of the combined references. There is nothing in these documents that would lead the skilled artisan to a formulation of a steroid in a propylene glycol/water solvent system whose pH is adjusted to the range of 3.5 to 5.0 by the addition of a strong acid thereto with the expectation of producing a nebulizable formulation that is very stable for prolonged periods of time. Accordingly, the invention as claimed is believed unobvious over the combined documents and withdrawal of the rejection is respectfully requested.

It is now believed that the application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Frederick D. Vastine, Ph.D.
Registration No. 27,013

Customer Number
22850
Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/03)